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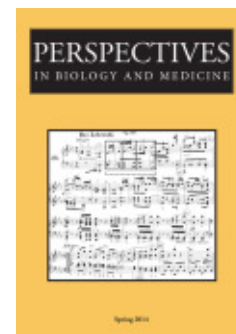
Prophet in His Own Country: Carlos Chagas and the Nobel Prize

Rachel Lewinsohn

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PROPHET IN HIS OWN COUNTRY

Carlos Chagas and the Nobel Prize

RACHEL LEWINSOHN

ABSTRACT In 1909, Carlos Chagas (1878–1934) discovered a new protozoon, *Trypanosoma cruzi*, and the (previously unknown) disease that it causes. Within a few months, virtually single-handed, he described the pathogen, its vector, and the clinical features of American trypanosomiasis (Chagas disease), a feat unique in medical history. He headed the Oswaldo Cruz Institute after the death of its founder (1917) until his own death; and from 1920 until 1926 he also directed the Brazilian Department of Public Health. His discovery brought him worldwide acclaim, but at home antagonism against Chagas, muted for years, finally flared up in a campaign that was acted out in the 1921–22 plenary sessions of the National Academy of Medicine. Chagas's name was repeatedly proposed for the Nobel Prize but he never received it; this hostile campaign may have been instrumental in costing him the award.

A prophet is not without honor, save in his own country, and in his own house.

—Matthew 13:57

Professor (ret.) of Internal and Tropical Medicine; Professor of History of Medicine, Faculty of Medical Sciences, State University of Campinas (SP)—UNICAMP, Brazil.

Correspondence: Caixa Postal 6033, 13083-970 Campinas, SP, Brazil.

Email: rachelew@unicamp.br.

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FIGURE 1

Carlos Chagas, 1932.

SOURCE: REPRODUCED BY KIND PERMISSION OF CASA DE OSWALDO CRUZ-FIOCRUZ, ARQUIVO E DOCUMENTAÇÃO, RIO DE JANEIRO, BRAZIL.

IT WAS IN APRIL 1909 THAT THE WORLD first took notice of the discovery of a new protozoon, *Trypanosoma cruzi*, and of an infectious disease caused by it. Early that year, both the trypanosome and the disease had been discovered by Carlos Chagas, a young physician working in the interior of the Brazilian state of Minas Gerais. To distinguish the new disease from the life-threatening African trypanosomiasis subsumed under the designation “sleeping sickness”—the infection (bovine as well as human) caused by the African *brucei* group of trypanosomes—he named it *American trypanosomiasis*.¹ But in 1910 the President of the National Academy of Medicine in Rio de Janeiro, Miguel Couto, proposed to name the disease after its discoverer: from that time on it has been known as Chagas disease.

Carlos Justiniano Ribeiro das Chagas (Figure 1) was born on 9 July 1878, in the neighborhood of Oliveira, a small town in the interior of Minas Gerais. His

¹In man, sleeping sickness, which is an infection of the central nervous system, is caused mainly by *Trypanosoma brucei gambiense* and, to a lesser extent, by *T. brucei rhodesiense*; *T. brucei brucei* does not produce human disease. All these trypanosomes are spread by species of the tsetse fly (genus *Glossina*), whereas the vector of *T. cruzi* is the bloodsucking barber or kissing bug (genus *Triatoma*, and others).

father, José Justiniano das Chagas, owned a modest coffee plantation; he died early, leaving his wife, Mariana Cândida Chagas, with four small children, of whom the eldest, Carlos, was only four years old. After her husband's death, despite great hardships, Dona Mariana succeeded in carrying on his work on the coffee plantation.

Carlos's childhood and youth were uneventful. His mother would have liked him to become a mining engineer, but one of his uncles, a medical practitioner of wide-ranging cultural interests, convinced him that if ever the country were to achieve economic independence, it had to rid itself of the countless endemic diseases that debilitated its manpower, blocking all progress. In 1896 Chagas entered the Medical School of Rio de Janeiro. Brazil was then a country of 10 million inhabitants; Rio de Janeiro, its capital, was a shabby, dirty, poverty-stricken town, despite its urban population of half a million.² Like all Brazilian ports at the time, Rio was one huge hotbed of infectious diseases, its unpaved streets crossed by open drains filled with a steady flow of excreta and all the filth of the town. Yellow fever, tuberculosis, and countless other diseases were rife, while smallpox and bubonic plague regularly appeared in epidemic waves. At all too frequent intervals, immigrant and native populations were decimated, precluding any kind of significant social or economic undertaking. Small wonder that the captains of European ships refused to berth in Brazilian ports.

At the turn of the 19th century, the Medical Faculty of Rio de Janeiro was undergoing a profound transformation: pathological anatomy and the practice of bedside teaching were introduced into the curriculum. Before long Chagas's talent for medical research became manifest. In the fifth year of his medical studies, he distinguished himself to such a degree that two of his teachers invited him to share in their activities: Miguel Couto, who was to become the greatest Brazilian clinician of his time, and Francisco Fajardo, who appointed Chagas his assistant and urged him to participate in his practical course on malaria. In 1902 he completed his academic studies with a thesis on the hematological aspects of malaria.

Although Chagas's contributions to malariology were later overshadowed by his discovery of *T. cruzi* and American trypanosomiasis, they are by no means negligible, including, as they do, the descriptions of the edematous form of quartan fever and of the bone lesions caused by malaria. Most important was his discovery that the infection is contracted indoors rather than out in the open. As a result of his findings, the disease came to be fought by means of caulking and the indoor application of natural pyrethrum. Fifty years later the validity of these practices was to be vindicated by the development and universal application of DDT and other synthetic residual insecticides.

The main targets of Chagas disease are the ganglia of the (parasympathetic) autonomic nervous system. None of the *brucei* species of trypanosomes is found outside Africa; hence sleeping sickness is confined to the African continent. There is no American sleeping sickness.

²In 1960 the capital of Brazil was transferred to Brasília in the Central Highlands.

Upon graduating from medical school, armed with a letter of recommendation from Fajardo, Chagas went to call on Oswaldo Cruz. Cruz was then engaged in the superhuman effort to stamp out the scourge of yellow fever, which perennially devastated the port and city of Rio de Janeiro. His mode of operation was the relentless fight against the mosquito, and the isolation of the victims in special hospitals. Receiving the young physician at Instituto Manguinhos (later to be renamed Instituto Oswaldo Cruz), he promptly invited him to join the Institute. But Chagas rejected the offer; instead, he took up clinical work at the Jurujuba Isolation (i.e., Pestilence) Hospital in Rio de Janeiro and in private practice. Three years later, however, compelled by financial problems, he accepted a commission to head an antimalarial campaign in the disease-ridden port of Santos, where the labor force was being decimated by malaria, seriously hampering construction work. Leaving his growing family in Rio, Chagas moved into the neighborhood of Santos, whence he directed the first successful campaign of its kind in Brazil. His achievement made it possible to complete the work that was to make Santos the largest port in South America.

He was 26 years old.

His success brought Chagas several similar assignments, followed by a renewed invitation to join Manguinhos. This time he accepted. He went on to train in protozoology and parasitology under the guidance of Oswaldo Cruz and some of the greatest scientists of the time, who were working at the Institute (Hartmann, Prowazek, and Giemsa, among others). It was a further antimalarial campaign, commissioned in 1907 by the Institute, that took him to Lassance in his native state of Minas Gerais, where the Central Railway was extending its lines into the interior; again, as in Santos, the work could not progress owing to malaria. This mission triggered the events that were to change his life.

A TALE OF DISCOVERY

On one of Chagas's trips inland towards the end of 1908, the railway engineers showed him and his travelling companion, Dr. Belisário Penna, a bloodsucking insect known locally as "barber bug," which usually bites its victim on the face, the part of the body most often uncovered during sleep (hence the name) (Figure 2). (The English term is "kissing bug.") "Once we heard of the blood-sucking habits of this insect," Chagas recalls in his "Historical Retrospect" (1922), "and of its proliferation in human dwelling-places, we became very interested in knowing its exact biology and above all in ascertaining if by any chance it were, as I immediately supposed, a transmitter of any parasite of man or of some other vertebrate." Dissection showed a flagellate protozoon in the hindgut of all the bugs, which Chagas identified as a previously unknown species of trypanosome; he named it *Trypanosoma cruzi* in honor of Oswaldo Cruz (Chagas 1922). The next steps were to find a vertebrate host of the parasite and to identify a disease that might be caused by it. He detected the flagellates in the peripheral blood of



FIGURE 2

The barber bug, Triatoma infestans. Average size of adult, 21–29mm.

SOURCE: REPRODUCED BY KIND PERMISSION OF THE VETERINARY PARASITOLOGY IMAGES GALLERY, INSTITUTE OF BIOMEDICAL SCIENCES, UNIVERSITY OF SÃO PAULO, BRAZIL.

domestic animals—a cat, a chicken—and then in the blood of a sick child, in whom he ultimately diagnosed the disease. Finally, in a rehearsal of Koch’s postulates, he reproduced the infection experimentally in small animals; rounding off the crucial demonstration, the trypanosomes were recovered and identified from these animals (Lewinsohn 1979, 1981).

Two brief communications announced the discovery in the prestigious German-language *Archiv für Schiffs- und Tropenhygiene* (Chagas 1909a, b). Subsequently, Chagas published several reports in the Institute’s journal, *Memórias do Instituto Oswaldo Cruz*, in which he described the morphology of the trypanosome, its cyclical development in its intermediate and definitive hosts, and the clinical features of the acute disease it caused in experimental animals and in man (Chagas 1909c, 1911; see also Chagas 1981; Chagas Filho 1993; Lewinsohn 1979).

The discovery was unique in a number of ways. In the first place, the entire achievement, whose foundations were laid down within a few months, was, to all intents and purposes, the work of one man. (Compare the history of 18 years’ research to discover the cause of malaria, a disease known since antiquity, described in vivid detail by Desowitz [1991]; or the brief description, by Coutinho and colleagues [1999], of the discovery of schistosomiasis, kala-azar, and malaria.)

Another striking feature of the discovery was Chagas’s unconventional approach to his task: he inverted the usual research protocol by starting out at the “wrong end,” so to speak. Instead of adopting the customary procedure which attempts to identify the cause(s) of a known disease, he began by won-

dering whether the bloodsucking bug, which he had casually been shown by the railway engineers, might not be an intermediate host and carrier of some parasite that might transmit a disease to man. Chagas's inversion of the common order of procedure may have been both cause and consequence of the fact that he carried out the research virtually by himself. He was well aware of the unusual nature of this approach:

These biological investigations were carried out in ways totally different from those which ordinarily lead to the aetio-pathogenic understanding of disease or which may add new morbid entities to the roster of those we know. . . . The verification of the disease, in this instance, was preceded by the discovery of the parasite that causes it; and when we observed the pathogenic flagellate in the peripheral blood of a feverish child, we already possessed complete knowledge of its biology, which we had ascertained in previous studies. (1922)

BERENICE

In April 1909, Chagas examined a baby girl who was burning with fever; her face and body were badly swollen and she had all the signs of an acute infection. This was 22-month-old Berenice: hers was the first human blood in which Chagas found the trypanosome, "the first proven case of human trypanosomiasis" (Chagas 1922). Figure 3 depicts the scene: the sick child, her face swollen, sitting on her mother's lap; the doctor in the shade of the rustic shack that was his surgery; in the background the disused railway wagon, Chagas's sleeping quarters and laboratory in Lassance.

For eight days the child had been running a high fever; then she "began to swell up," and her mother took her to the doctor. Chagas describes his findings: temperature 40°C; signs of an acute toxemic infection; liver and spleen enlarged; peripheral lymph nodes engorged. The most significant sign was a hard subcutaneous swelling on the child's face and body: this was the myxedematous infiltration that came to be known as one of the most characteristic signs of the acute form of Chagas disease. A fortnight or so before Berenice was brought to him, Chagas had spent a night in the bug-infested hut where she lived with her parents. There he had found a cat infected with *T. cruzi*: "and I had occasion to observe a large number of insects biting the people who lived there, including the child who was now febrile [but] who was then in perfect health."

Examination between cover-glass and slide revealed the presence of flagellates in goodly number; . . . the fixing and staining of blood films made it possible to characterize the morphology of the parasite and to identify it as Trypanosoma cruzi. . . . Thus the existence of a new human trypanosomiasis was confirmed, the second to be known, whose parasite showed well-defined morphological and biological characteristics, entirely different from those which distinguish other species of the same genus. . . . There remained now to be carried through careful studies as to the patho-



FIGURE 3

Chagas examining a baby girl, possibly Berenice (1909).

SOURCE: REPRODUCED BY KIND PERMISSION OF CASA DE OSWALDO CRUZ-FIOCRUZ, ARQUIVO E DOCUMENTAÇÃO, RIO DE JANEIRO, BRAZIL.

genesis, symptomatology, epidemiology and the geographic distribution of the disease, which I had discovered in its acute form. Was it always like this or did it show well-defined chronic forms? My clinical experience and knowledge of the unusual condition of the local inhabitants led me to admit that in this trypanosomiasis, besides the acute form, other chronic ones awaited detection and description. (Chagas 1922, emphasis in original)

In his thoughtful analysis of the African and American trypanosomiasis, Ormerod (1979) points out that all the symptoms and many of the physical signs found in Chagas disease are common to other infections. Thus Berenice's acute febrile illness might well have been malaria, which was rampant in Minas Gerais. Indeed, when her parents brought her to be examined by Chagas, they believed that the child was ill with it.

On more than one occasion, Chagas comments on the difficulty of classifying the symptomatology he found in Minas Gerais. Ormerod thinks it the more remarkable that in an area riddled with parasitic disease of every kind, where most of the symptoms, above all in children, might well be associated with kala-azar, hookworm, malaria, kidney disease, or malnutrition, the new disease stood out so clearly in Chagas's mind as to assume an identity in its own right (Ormerod 1979).

Chagas himself saw many children die of the acute form of the disease.

Berenice, however, survived. In his case notes he wrote: "The patient went home. Eight days later, parasites were still seen in her blood and the swelling persisted. . . . Subsequent observations showed the benign evolution of the acute aspects, and the disease became chronic in character" (Chagas 1916, pp. 45–46). When he saw her for the last time, Berenice's temperature had dropped to normal and the trypanosomes had disappeared almost completely from the peripheral circulation. Thereafter, he lost track of her.

But the story does not end there, although Chagas, unfortunately, did not live to see its sequel. Incredible though it may seem, 27 years after his death and 52 years after she had been examined by him, Berenice, now middle-aged and in good health, was found to be living with her family—husband, son, daughter-in-law, and three grandchildren—on a farm in Pirapora (Minas Gerais). At the request of a group of doctors of the Medical Faculty of the Federal University of Minas Gerais, who established beyond doubt that she was the same person in whom, as an infant, Chagas had first diagnosed American trypanosomiasis, she entered the Teaching Hospital in Belo Horizonte and submitted to a thorough examination. No lesions were found, but her blood tests were still positive for Chagas disease. (Salgado et al. 1962). Berenice died in 1981 in Pirapora (MG), aged 73 years, presumably of natural causes (Lewinsohn 1982).

Blind chance has often been advanced (particularly by those less favored by talent or fortune) as a putative explanation of some great discovery or other outstanding achievement. Inevitably, this was said of Chagas: that he stumbled by sheer luck on the vector of *T. cruzi*, the parasite, and the disease that was to bear his name. But even a cursory glance at his writings ought to convince the reader that chance played no more than a minor role, if any at all, in the discovery of Chagas disease. "*Dans les champs de l'observation*," says Louis Pasteur, "*le hasard ne favorise que les esprits préparés*." If ever a "mind was prepared" to recognize the significance of unusual phenomena, it was that of Chagas; very likely his wide experience with malaria, another vector-borne disease, gave direction to his thoughts.

In recent years there have been several attempts to show that the disease was known before Chagas became aware of it. No doubt many of the *symptoms* had long been known. For instance, *mal de engasgo* (choking sickness, megaesophagus) was described in 1855 to the Reverend J. C. Fletcher by Dr. J. C. Reinhardt, a physician living in Brazil at the time, who stated that "he had never read anything about the disease, and that he intended to study it in order to present the result to the medical world" (Meneghelli et al. 1998). "Too bad he didn't do it," is the authors' comment. Too bad indeed; but there is not the slightest hint that Dr. Reinhardt associated the choking sickness with any of the other (especially, cardiac) manifestations of Chagas disease, or with the bite of the bloodsucking bug. Thus, while its symptoms were well known, the disease (let alone its cause) awaited identification and description.

There were other such observations, fragmentary and unrelated; all of them led nowhere. Nor am I inclined to give much weight to the argument that, if

Chagas had not discovered the disease, someone else would have done so. Perhaps. Certainly the time was unusually favorable for biological research: the biological revolution that spanned a few decades before and after the turn of the 19th century and witnessed the birth of a large number of new scientific disciplines was highly propitious to research on infectious diseases. Politically, also, the time favored such research: witness the schools of tropical medicine that were founded in many industrialized countries at the turn of the 19th or the beginning of the 20th century, in consequence of European and North American colonial expansion in tropical countries. But there can be no certainty of the direction that any investigation may take; and when all is said and done, the indisputable fact is that it was Chagas who discovered *T. cruzi* and described American trypanosomiasis.

Finally, it is worthy of note that Chagas was trained entirely in Brazil, at a time when the country had little claim to a tradition in medical science such as was already being practiced in Europe, and when research at Manguinhos was in its infancy (Lewinsohn 1979; Stepan 1976).

SUCCESS—AND CONFLICT

Chagas's discovery brought him immediate, worldwide acclaim, as described by his son in *Meu Pai* and in his autobiography (Chagas Filho 1993, 2000).³ Honors were showered upon him: in 1912 he won the coveted Schaudinn Prize, awarded every four years by the Hamburg Institute for Tropical Diseases for the world's best work in parasitology and tropical medicine. Chagas was the second scientist to be so honored; the first had been Stanislaus von Prowazek.

Why did the description of the American trypanosome arouse such keen, universal interest? One of the reasons may well have been the hope it raised in the scientific community that the new findings might throw some light upon the *brucei* species of trypanosomes and the diseases caused by them. Up to the time of Chagas's discovery, the African trypanosomiasis were the only ones known to exist; ravaging great regions of the continent colonized by the European powers, they had become a source of the gravest concern to the metropolitan governments. Thus it is the African diseases, and the little that was known about sleeping sickness, that may partly explain the worldwide interest in the new trypanosome.

³Chagas Filho, who died in February 2000 aged 89, was himself a prolific writer and a celebrated biophysicist whose countless titles and awards attest to his distinguished career in research and teaching. Appointed Brazilian ambassador to the United Nations, he was active in UNESCO, WHO, and PAHO. Like his father, Chagas Filho was a great humanist; unlike him, he was a practicing Catholic. Pope Paul VI appointed him in 1972 to preside over the Vatican's Pontifical Academy of Sciences, an office he held for 16 years. Throughout his life he fought for recognition in Brazil and Latin America of his father's work, above all stressing the enormous socioeconomic importance of Chagas disease in terms of public health as well as human suffering.



FIGURE 4

Einstein visits Carlos Chagas at Manguinhos, 1925.

SOURCE: REPRODUCED BY KIND PERMISSION OF CASA DE OSWALDO CRUZ-FIOCRUZ, ARQUIVO E DOCUMENTAÇÃO, RIO DE JANEIRO, BRAZIL.

Be that as it may, Chagas became a celebrity overnight. Universities, medical faculties, and research institutes all over the world vied with invitations and proffered titles and honors; in 1925 he was elected to the League of Nations' Committee of Hygiene, a forerunner of the World Health Organization, whose seat at the time was in Paris. When Albert Einstein (to name but one of the illustrious personages with whom he became acquainted) came to Brazil in 1925, he visited Chagas at the Oswaldo Cruz Institute (Figure 4). Inevitably, Chagas's name was proposed for the Nobel Prize.

But whereas the whole world celebrated his achievements, the overwhelming success of the young scientist from the backwoods of Minas Gerais set off a reaction of a different kind in some of his colleagues at Manguinhos, the Faculty and the National Academy of Medicine. While Oswaldo Cruz and most of the Institute's staff gloried in Chagas's fame, others viewed his rapid advancement at the Institute with jaundiced eyes. By November 1916, when he went abroad for the first time to attend a medical congress in Buenos Aires, antagonism against him, mute and covert until then, began to flare up. His stay in Argentina was marred by an unpleasant incident involving Rudolph Kraus, Director of the Institute of Bacteriology at Buenos Aires, and Chagas's own laboratory at Manguinhos. Kraus had denied the existence of American trypanosomiasis in Argentina. On a

visit to his laboratory, Chagas was shown some specimens of human and animal tissues with evident Chagasic lesions. The wooden boxes they were packed in left no doubt of their origin: the (anonymous) sender was a colleague of Chagas's at Manguinhos. Until questioned by a puzzled Kraus, who had not solicited them, Chagas had been ignorant of the matter.

The existence of Chagas disease, one of the main issues raised in the 1922–23 debate at the National Academy of Medicine, had never been questioned by any other non-Brazilian scientist. Now, judging by the incident of the uncalled-for samples sent to Kraus, and bearing in mind the *dramatis personae* involved in the anti-Chagas campaign, the suggestion may not be too far-fetched that it may have been a Brazilian who planted the seed of doubt in the mind of the German bacteriologist.

Much has been made of the “battle” between Chagas and Kraus, though with hindsight it might rather be called a tempest in a teapot. The issue in question was the negative result of two surveys for evidence of Chagas disease (and goiter), carried out by Kraus and two colleagues in the Argentine Chaco (Kraus 1926; Kraus, Rosenbusch, and Maggio 1915). Actually, Kraus was less interested in Chagas disease itself than in its putative association with endemic goiter.⁴ At a special session of the medical congress, he stated that despite the presence in the region of large numbers of infected kissing bugs, no evidence had been found of human Chagas disease. No doubt one reason for this was Kraus's faulty technique—two to three weeks after infection takes place, the flagellates are no longer found in the peripheral blood (Benchimol and Teixeira 1993)—but Chagas preferred to counter that the parasites had not yet become adapted to their human hosts. Moreover, diagnosis of the disease was difficult. Convinced by Chagas's arguments, Kraus “publicly congratulated his opponent and declared that . . . reason was on the side of Manguinhos” (Chagas Filho 1993, p. 191). Indeed, when Mazza and Romaña surveyed northern Argentina for Chagas disease 20 years later, they found over a thousand cases in the Chaco alone (Carneiro 1963.)

Back from the Argentine, a grotesque accusation was in store for Chagas: because he openly discussed the disease and its implications, “which was bound to damage the reputation of Brazil among more advanced nations,” he was reproached with being unpatriotic; this stupid, pointless charge was to haunt him for many years.

Chagas returned to Brazil to find that Oswaldo Cruz, who had long been ailing, was dying. Upon Cruz's death in February 1917, the President of the Republic appointed Chagas Director of the Institute, a post he held until his own

⁴It was an unfortunate coincidence that when Chagas made his discovery, the distribution in Minas Gerais of endemic goiter and Chagas disease was very similar, which led him to conclude that the disease might be identical with thyroiditis. For years he was undecided on the matter. The error was only cleared up in the 1930s (see Lobo 1968).

death in 1934. This was a bitter pill for Figueiredo Vasconcellos, his senior at Manguinhos, who had been running the Institute during Cruz's last illness and had confidently expected to succeed him as its Director. Chagas Filho (1993) suggests this was the main reason for Figueiredo's hatred of Chagas. The bitter enmity of Afrânio Peixoto may have been caused or exacerbated by a similar motive involving the directorship of the Department of Public Health, held by Chagas between 1920 and 1926. Though Peixoto's medical career was undistinguished, he achieved some notoriety in his time as a novelist and *littérateur* (today he is almost forgotten even as a writer). He harbored political ambitions, instigated, no doubt, by his social rank and literary success; the Department of Public Health, whose directorship held ministerial rank, would have been a stepping stone to higher things. Thwarted in his aspiration, Peixoto became the covert leader of the campaign against Chagas. When in 1922 the battle was finally joined at the National Academy of Medicine, Peixoto never appeared in public, but acted through his followers, an *éminence grise* pulling strings and writing endless vitriolic letters to the President of the Academy. By virtue of his rhetoric and his social position, he attracted not only Figueiredo Vasconcellos and others who felt they had been pushed aside by Chagas, but every disaffected, malcontent physician or researcher who, aware of his own shortcomings, would not or could not stomach Chagas's genius. Moreover, Peixoto held the chair of Hygiene at the Rio de Janeiro Medical School, and some sectarians of his were *hygienists*, inveterate (though somewhat belated) followers of the *Grundwasser* school of Pettenkofer.⁵ As such they were opposed to the theories of Pasteur and Koch, which by then had won the age-old battle of contagionism versus miasmaticism, and were of course dominant at Manguinhos.

THE CAMPAIGN

The brief account that follows can give but a faint idea of the antagonism Chagas had to contend with. In Brazil, then as now, politics of all kinds and the struggle for power and public funding bedeviled any undertaking relative to medicine, science, and research. A thorn in the flesh of power-hungry bureaucrats was the financial autonomy that Oswaldo Cruz had been able to secure for the Institute and that Chagas had been able to maintain. There were also unending rivalries between Manguinhos on the one hand, and, on the other, the Rio de Janeiro Faculty of Medicine, and Instituto Butantan in São Paulo (Benchimol and Teixeira 1993; Perleth 1997).

The campaign against Chagas was a long-drawn-out attempt by an envious clique to blacken the name of Brazil's greatest scientist (Lewinsohn 2003). There

⁵After his disastrous attempt at intervention in the 1892 cholera epidemic in Hamburg, which sealed the success of Koch's theories, Pettenkofer's unquestioned authority waned. The wreck of his life's work led him to commit suicide in 1901.

was never any question of a truly scientific inquiry, which—far from disturbing or vexing Chagas—would certainly have been welcomed by him. His son observes that although the smear campaign affected neither his father's reputation nor his situation at the Department of Public Health and Manguinhos, Chagas's health was shaken and his peace of mind disturbed for a long time. Chagas Filho attributed the beginning of the heart disease that was to carry his father off 12 years later to the unending stress of the years of attacks on him and his work.

After years of underground burrowing by Peixoto and his coterie, and veiled or open attacks casting doubt on Chagas's honesty and his activity as Director both of Manguinhos and the Department of Public Health, the campaign exploded on 6 December 1922, in an extraordinary session of the National Academy of Medicine. Among other preposterous accusations, his opponents alleged: (1) that Chagas had invented a disease that did not exist; (2) but if it did exist, it was restricted to the small area in Minas Gerais where he had found his first cases; (3) moreover, if it did exist, the number of cases did not exceed some 40 patients "or a few more," whom he had brought to Rio de Janeiro, to be examined by his skeptical colleagues; and (4) that the real discoverer of the flagellate *T. cruzi* was not Carlos Chagas, but Oswaldo Cruz.

In a desperate attempt to resuscitate Kraus's disclaimer (which he had publicly withdrawn), Chagas's opponents insisted on repeating that the disease was non-existent in regions heavily infested with kissing bugs, even though the bugs might harbor the flagellates. Similarly, they never tired of repeating the ridiculous charge, already mentioned, that Chagas had been guilty of unpatriotic behavior by divulging the facts about the disease.

Alternating between malicious and absurd fabrications, the attacks dragged on and on at the Academy, until yet another extraordinary session put a stop to them exactly one year after the start of the campaign, and the efforts of Chagas's opponents came to naught on every count. Ironically, the final effect of the cabal turned out to be the exact opposite of what they had intended, for the campaign's net result was to highlight the greatness of the achievement they had tried to denigrate.

The close of the debates resembles nothing so much as the happy ending of a movie of suspense, with its obligatory trial scenes: the good guy comes out triumphant; the bad guys are defeated: once again virtue has dramatically prevailed. But the fact that Chagas won the day should not blind us to the true significance of the campaign, its causes, and its effects. The price that the good guy, and, in the final analysis, Brazil and science, had to pay for victory, was outrageously high. However distressing the campaign and its sequelae may have been for Chagas and his family, the consequences for Brazil and for medical science were nothing short of disastrous. The National Academy and the Faculty of Medicine—indeed, the entire medical profession of Brazil—all came out tainted. Moreover, in addition to incalculable economic losses, the campaign resulted in the irretrievable loss of many years of research and teaching on Chagas disease.

To appreciate the harmful effects of the campaign in terms of the study of Chagas disease, it must be noted that although the disease was soon included in the medical textbooks in the German, French, and English languages, and was taught in the most prestigious medical schools of the world, in Brazil—incredible though it may seem—all mention of it was banned both from books and classrooms for years on end. As an inevitable, tragic consequence, research on Chagas disease came to a virtual standstill. The campaign had failed to prove the nonexistence of the disease (or alternatively, its insignificance), but instead of recognizing the validity of the proofs to the contrary, the Medical Faculty decided to ignore everything. The effect on medical teaching in Brazil was predictable. Year after year the schools turned out physicians who graduated without ever having heard of Chagas disease. They learned all that was known about sleeping sickness, but nothing at all about the endemic, catastrophic scourge that ravaged their own country and subcontinent. And since they were not aware of its existence, how were they to diagnose, let alone study it? According to Chagas Filho (1993), “At the Faculty [of Medicine, Rio de Janeiro], only one professor of clinical medicine, probably because he was a cardiologist, lectured on the cardiac form of Chagas disease. He was Genival Londres. However, one of the most famous cardiologists of Rio de Janeiro continued to deny the existence of Chagas disease.” It is impossible to reckon the cost to the health of the Brazilian people, whose suffering, if not prevented, might at least have been mitigated if the disease had not been wantonly ignored by the medical establishment. It was only after Chagas’s death in 1934 that the medical community of Brazil finally recognized the existence of Chagas disease. The renewed interest was kindled by the studies of the two Argentine researchers, Cecilio Romana and Salvador Mazza.

Although Chagas was convinced of the importance of his discovery, not even he could have foreseen the enormous incidence or the social and economic impact of Chagas disease on the American continent, let alone the possibility of its spreading to the rest of the world.⁶ The surveys that finally elucidated its continental incidence became possible only after the widespread introduction of electrocardiography, shortly before World War II. To all intents and purposes, the disease is incurable; and since it is easily transmitted by blood transfusion, it may flare up in the victim (even a “silent” carrier) in its acute, fulminant form, causing sudden death. Thus, there is no need to belabor the threat to public health represented by millions of asymptomatic carriers, in Central and South America

⁶The WHO currently estimates the incidence of Chagas disease in Latin America as follows: total of individuals infected (the vast majority asymptomatic carriers), 18.5 million; at risk, 91 million. In Brazil alone it is estimated that 3 to 5 million harbor the infection; some estimates go as high as 8 million infected. Asymptomatic carriers in the United States and Canada (of whom the overwhelming majority are immigrants from the southern hemisphere) are estimated at roughly 100,000 to 150,000 (Hagar and Rahimtoola 1991; Holbert et al 1995; Kirchoff 1993; Wanderley and Corrêa 1995).

and abroad, who may donate blood without having the faintest suspicion of harboring the disease.

These problems, which have been a devastating presence in Latin American countries for nearly a century, have more recently become a source of concern to the northern hemisphere, owing to the intense migration from the southern subcontinent to the United States and Canada. Indeed, whereas in the past “American trypanosomiasis” in effect denoted its localization to South and Central America, today, owing to the ease and speed of intercontinental travel, no country or continent can consider itself exempt from risk. Add to this the tragic paradox, that the danger of transmission not only of Chagas disease, but also of AIDS and other such infections, has been magnified by the advances of biotechnology: blood transfusion, now an everyday expedient all over the world, from a life-saving medical procedure has become one endangering life.

CARLOS CHAGAS AND THE NOBEL PRIZE

Three attempts were made to obtain the Nobel prize for Chagas. He was nominated for the prize in 1913 by Pirajá da Silva, and again in 1921 by Hilário de Gouvêa; in 1932 renewed efforts were underway in Europe, headed by the Spanish hematologist Gustavo Pitaluga, to obtain the prize for him. However, Chagas died in November 1934.

Why was he denied the prize? Countless people have puzzled over the question why one of the outstanding scientists of the 20th century was never awarded the highest honor that humanity can bestow. Many investigations over the years, including several exhaustive reviews, by Carlos Chagas Filho and others, have yielded no information on the subject. However, one or two comments are worth noting. It has been suggested that the indication of 1913 may have been premature, while the last attempt could not be brought to fruition: the prize is not awarded posthumously. Scrutiny, therefore, has focused on the indication for the prize of 1921. Although it was thought unlikely that at this stage new facts might crop up, the search for information continued. It was Professor João Carlos Pinto Dias, a lifelong Chagas scholar, lecturer, and senior researcher at Fiocruz (Fundação Instituto Oswaldo Cruz), Belo Horizonte, who drew my attention to the two items that follow.

It appears that a few years ago an exposé concerning Chagas was found in the archives of the Oswaldo Cruz Institute (Manguinhos) in Rio de Janeiro. Dated 1920 and written in English, it sets out the “reasons for the presentation of Dr. Carlos Ribeiro Justiniano das Chagas as a candidate for the Nobel Prize in Medicine.” The (anonymous) author states that Chagas’s curriculum vitae and an ample justification of his candidacy for the 1921 prize were presented to the Nobel Committee, emphasizing his scientific merits and his genius, and laying particular stress on the importance of his discovery for all mankind, especially for the peoples of Latin America. Neither the Chagas family nor the archives of

Manguinhos can shed light on the further proceedings (if indeed there were any), or the reasons why the prize was not awarded to him.

However, there is a further tantalizing twist to the story. A biography of the Argentine researcher Salvador Mazza, published by the historian-physician Jobino Pedro Sierra-Iglesias (1990), contains the following account:

In 1921 [Chagas] was proposed for the Nobel Prize in Medicine, and when everything pointed to its being awarded to him, unconscionable influences [*inconfesables influencias*] intervened. The Swedish Institute had approached scientific organizations in Brazil for information on [Chagas's] personality and his work; but some of his own countrymen (including, incredibly, some who were not physicians, and thus in principle lacked the qualifications to form a valid judgement of the discovery of [American] trypanosomiasis), advised against [the prize being given to Chagas]; in that year the coveted world prize for medicine was not awarded to anyone.⁷

In an attempt to discover the basis of these assertions by Sierra-Iglesias, on a visit to Argentina, Professor João Carlos Pinto Dias and Professor José Rodrigues Coura (Director of Fiocruz in Rio de Janeiro), called upon the author, who “regrettably had nothing further to add to what he had written. He merely told us that the information had come from Salvador Mazza [d. 1946] and the Uruguayan scientist R. Talice, a contemporary of Carlos Chagas, who unfortunately died last year in Montevideo” (Dias, personal communication).

Why was Chagas not awarded the Nobel Prize? Although there is no evidence in Brazil to lend support to the assertions of Sierra-Iglesias (1990), Professor Dias believes (and I agree) that the interpretation of the Argentine historian is probably correct. It is quite likely that the “scientific organizations in Brazil” that were approached by the Committee were influenced by Chagas’s opponents, and that their unfavorable advice was a direct outcome of the campaign waged against him. It is even more likely that the consultation, whomever it may have been addressed to in the first place, ended up in the National Academy of Medicine, which was after all the country’s greatest medical authority—and the stronghold of Chagas’s enemies. If that was indeed the case, the outcome was entirely predictable. Finally, it is reasonable to assume that the members of the Nobel Committee were undecided, because in 1921 the (Brazilian) medical establishment had not yet accepted the existence of Chagas disease.

This was the opinion of Chagas Filho, expressed to me in an interview in July 1999: “There have been questions raised as to why my father was not awarded the Nobel prize. But I ask you, how could the Swedish committee award him the prize, when Chagas disease was being argued about . . . worse, its existence was being denied outright . . . ?” And, further: “Also because the great-

⁷It has not been possible to find out whether there were other candidates for the 1921 Nobel Prize for Medicine.

est medical authority of Brazil, the National Academy of Medicine, allowed the discussion about the existence or nonexistence of the disease to go on and on . . . To this day we do not know how many of our faculties of medicine never taught Chagas disease.”

There have been other great men and women, of course, who failed to receive the Nobel Prize, though unquestionably deserving of it. The reasons that induce the Nobel Committees to deny the award are numerous and varied (see, for example, the case of Lise Meitner [Crawford et al. 1997]). As for Carlos Chagas, in the final reckoning it is more than likely that, directly or indirectly, it was the campaign against him, engendered by envy, hatred, and mediocrity, that caused the prize to be denied to Brazil’s greatest scientist. He may not have been the only victim of his egregious countrymen and their perverse pleasure in depriving a great compatriot of the prize. In the 1970s, when the Nobel prize for peace was about to be awarded to the great libertarian archbishop of Recife and Olinda, Dom Helder Câmara, fierce protest by the Brazilian government (then a military dictatorship) put a stop to the proceedings.

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